Multiple Recognition of Polyamine-Bridged Cyclodextrin Dimers

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Abstract. The binding properties of two polyamine-bridged β-cyclodextrin dimers were studied by fluorescence and UV-Vis spectroscopy. The linkers of the dimers can recognize metal ions and the complexation may enhance the cooperative binding ability of the dimers for the ditopic substrate 6-(p-toluidino)-2-naphthalenesulfonic acid (TNS).

Key words: cyclodextrin dimer; multiple recognition; association constant; coordination.

1. Introduction

As a typical host molecule designed for the purpose of mimicking the multiple recognition in enzymatic catalysis, cyclodextrin (CD) dimer is capable of encapsulating appropriate ditopic substrates cooperatively, with stronger binding ability and selectivity than simple CD molecules [1, 2]. In the case of a bridge containing another functional group, triple recognition may be achieved and the binding ability and selectivity of the host are further enhanced [3–8]. Metal ions often play a critical role in triple recognition, they can coordinate with the linkers, thus interact with substrates as binding or catalytic groups.

We are interested in developing cyclodextrin dimers linked by flexible polyamine chains and investigating their binding properties [9, 10]. Since polyamines can bind transition metal ions feasibly with specific space configuration, we expected that a long, flexible polyamine linker could become short and rigid after recognizing metal ions. Thus, as compared with that in the absence of metal ions, the binding ability of the dimer could be different or even increased, especially for appropriate shorter substrates such as 6-(p-toluidino)-2-naphthalenesulfonic acid (TNS). β-Cyclodextrin dimers **1** and **2** are two examples. Here we report their binding properties.

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Table I. Association constants for complexes of dimers and TNS.

Species	[Dimer] (M)	Excitation λ (nm)	λ_{max} (nm)	K_a (M^{-1})
Dimer **1**, TNS	8.25×10^{-6} to 6.17×10^{-4}	330	453.6	$(1.07 \pm 0.21) \times 10^4$
Dimer **1** – Ni(II), TNS	8.25×10^{-6} to 2.47×10^{-4}	320	455.6	$(3.10 \pm 0.11) \times 10^4$
Dimer **2**, TNS	1.00×10^{-5} to 4.00×10^{-4}	318	452.4	$(9.05 \pm 0.81) \times 10^3$
Dimer **2** – Ni(II), TNS	1.00×10^{-5} to 4.00×10^{-4}	320	451.2	$(1.00 \pm 0.07) \times 10^4$
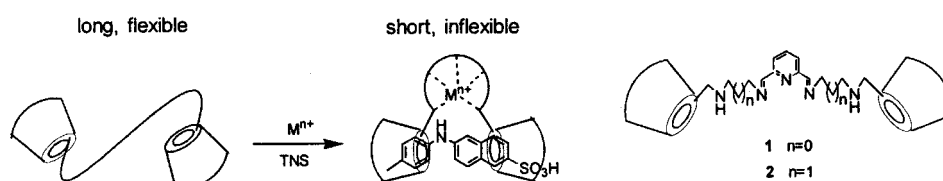
2. Experimental

The dimers were prepared as reported previously [10]. Fluorescence experiments were conducted in 10 mM HEPES (N-(2-hydroxyethyl)piperazine-N'-ethanesulfonic acid) buffer (pH = 7.0) at 25 °C using TNS as guest molecule. To study the effect of metal ions on the cooperative recognition, fluorescence spectra were measured at a constant concentration of TNS on addition of various amounts of dimer both in the absence and presence of Ni(II). In the latter case, Ni(OAc)$_2$ was added as a five-fold amount of CD dimer in every measurement. The concentration range of the dimer, excitation wavelength and maximum emission wavelength for each system are listed in Table I.

UV-Vis spectra were measured in 10 mM HEPES buffer (pH = 7.0) at 25 °C, using the continuous variation method with a total concentration of Ni(II) and the dimer of 4.0×10^{-3} M.

3. Results and Discussion

Double reciprocal plots of the fluorescence titration data are shown in Figures 1 and 2. It is obvious that the data gave straight lines. The association constants (K_a) were calculated from the slopes and intercepts in Figures 1 and 2 according to the literature [11], and the results are listed in Table I.

As the long and flexible bridges do not match the relatively short substrate TNS, originally we did not expect that the dimers without metal ions could bind TNS more tightly than β-CD. However, it was found that this was not the case. The K_a
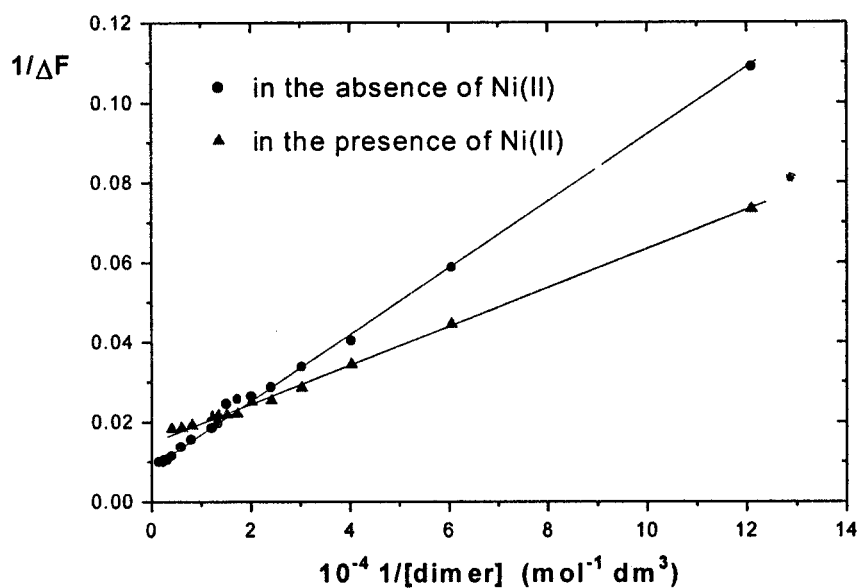
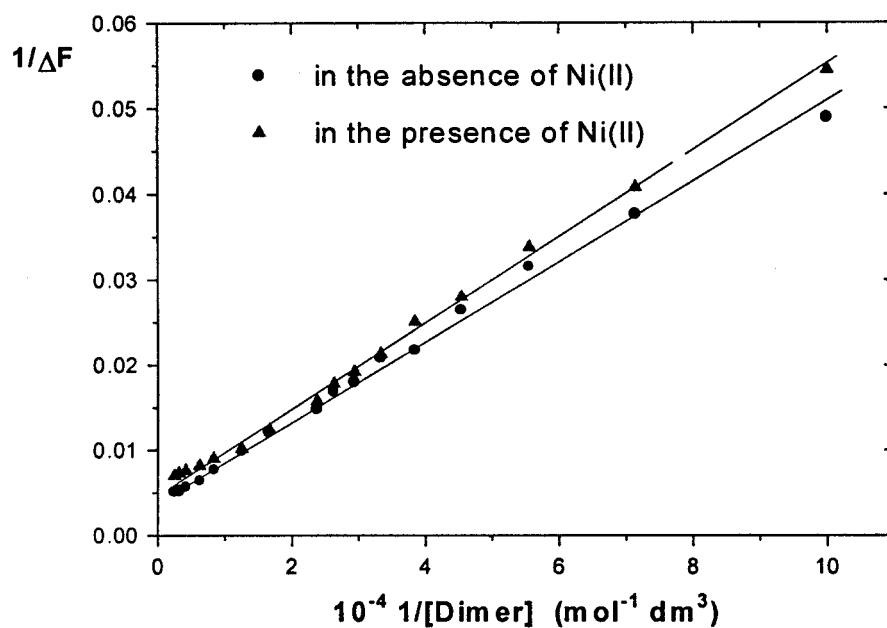*Figure 1.* Double reciprocal plots of the titration data for dimer **1** and TNS. ([TNS] = 1.00 ×
10^{-5} M).

Figure 2. Double reciprocal plots of the titration data for dimer **2** and TNS. ([TNS] = 1.00 ×
10^{-5} M).

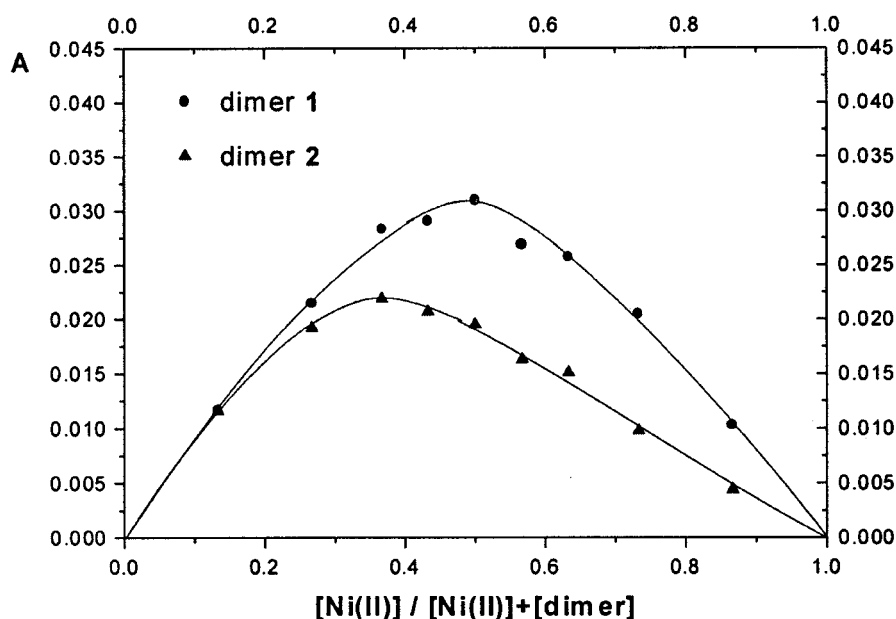*Figure 3.* Job's plots of the coordination of the dimers with Ni(II). ([Ni(II)] + [dimer] = 4.0 × 10^{-3} M, 10 mM HEPES buffer, pH = 7.0, 25 °C).

values for the TNS-complexes of the dimers are far higher than the previously reported values for the binary complex of β-CD (1200 to 3950 M^{-1}) [12], indicating that cooperative recognition of TNS by the dimers is substantial. The complex of dimer **1** is a little more stable than that of dimer **2**. This result is consistent with the previous discovery that shortening of the linker is advantageous for binding [12, 13].

After adding Ni(II), dimer **1** showed an obviously increased ability for binding TNS, with a K_a value three-fold higher than that without metal ions. However, it is surprising that such an enhancement was not obtained when dimer **2** with nickel ion was investigated. In order to understand the result clearly, we studied the complexation of the dimers with Ni(II) by absorbance spectra using the continuous variation method. Job's plots of the coordination data at 930 nm are shown in Figure 3. They indicate that the coordination of dimer **1** with nickel ion forms a 1 : 1 host-guest complex, while a 2 : 1 complex is formed with dimer **2**. In the possible configuration of the complex of dimer **1**, all the nitrogen atoms in the linker coordinate to a nickel ion, folding the linker and dragging the two CD cavities close. Evidently, it is favorable for the binding of TNS.

dimer1-Ni(II) (possible structure)

dimer2-Ni(II) (possible structure)
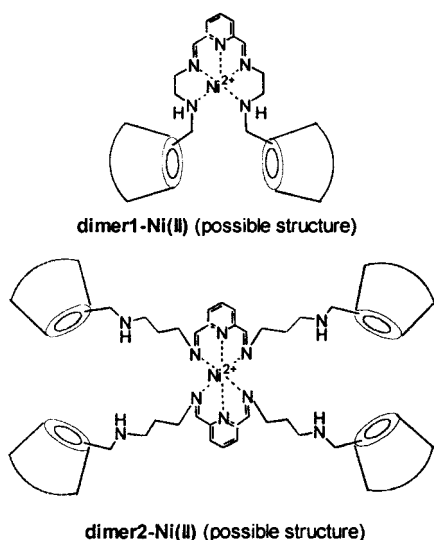
However, in the complex of dimer **2** with Ni(II), there is a suggestion that the pyridino groups in the linkers of the two dimers are engaged in the coordination. Compared with the circumstance in the absence of metal ions, neither the length nor the flexibility of the linker is changed much. Therefore, it is understandable that dimer **2**-Ni(II) could not bind TNS more strongly than dimer **2** alone.

Acknowledgement

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